

SEQUENCE LISTING



<110> Charette, Marc F.  
Rueger, David C.  
Higgins, Dennis  
<120> ENHANCEMENT OF MORPHOGEN ACTIVITY  
<130> 00960-569 NATL  
<140> 09/509,648  
<141> 2000-10-05  
<150> PCT/US98/22655  
<151> 1998-10-26  
<150> 60/063,624  
<151> 1997-10-27  
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<170> PatentIn Ver. 2.1  
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Met His Val  
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cgc tca ctg cga gct gcg gcg ccg cac agc ttc gtg gcg ctc tgg gca 105  
Arg Ser Leu Arg Ala Ala Ala Pro His Ser Phe Val Ala Leu Trp Ala  
5 10 15  
ccc ctg ttc ctg ctg cgc tcc gcc ctg gcc gac ttc agc ctg gac aac 153  
Pro Leu Phe Leu Leu Arg Ser Ala Leu Ala Asp Phe Ser Leu Asp Asn  
20 25 30 35  
gag gtg cac tcg agc ttc atc cac cgg cgc ctc cgc agc cag gag cgg 201  
Glu Val His Ser Ser Phe Ile His Arg Arg Leu Arg Ser Gln Glu Arg  
40 45 50

cg <sup>g</sup> gag atg cag cg <sup>c</sup> gag atc ctc tcc att ttg ggc ttg ccc cac cg <sup>c</sup>		249
Arg Glu Met Gln Arg Glu Ile Leu Ser Ile Leu Gly Leu Pro His Arg		
55	60	65
ccg cg <sup>c</sup> ccg cac ctc cag gg <sup>c</sup> aag cac aac tcg gca ccc atg ttc atg		297
Pro Arg Pro His Leu Gln Gly Lys His Asn Ser Ala Pro Met Phe Met		
70	75	80
ctg gac ctg tac aac gcc atg gc <sup>g</sup> gtg gag gg <sup>c</sup> ggc ggg ccc gg <sup>c</sup>		345
Leu Asp Leu Tyr Asn Ala Met Ala Val Glu Glu Gly Gly Pro Gly		
85	90	95
gg <sup>c</sup> cag gg <sup>c</sup> ttc tcc tac ccc tac aag gcc gtc ttc agt acc cag gg <sup>c</sup>		393
Gly Gln Gly Phe Ser Tyr Pro Tyr Lys Ala Val Phe Ser Thr Gln Gly		
100	105	110
ccc cct ctg gcc agc ctg caa gat agc cat ttc ctc acc gac gcc gac		441
Pro Pro Leu Ala Ser Leu Gln Asp Ser His Phe Leu Thr Asp Ala Asp		
120	125	130
atg gtc atg agc ttc gtc aac ctc gtg gaa cat gac aag gaa ttc ttc		489
Met Val Met Ser Phe Val Asn Leu Val Glu His Asp Lys Glu Phe Phe		
135	140	145
cac cca cg <sup>c</sup> tac cac cat cga gag ttc cg <sup>g</sup> ttt gat ctt tcc aag atc		537
His Pro Arg Tyr His His Arg Glu Phe Arg Phe Asp Leu Ser Lys Ile		
150	155	160
cca gaa ggg gaa gct gtc acg gca gcc gaa ttc cg <sup>g</sup> atc tac aag gac		585
Pro Glu Gly Glu Ala Val Thr Ala Ala Glu Phe Arg Ile Tyr Lys Asp		
165	170	175
tac atc cg <sup>g</sup> gaa cg <sup>c</sup> ttc gac aat gag acg ttc cg <sup>g</sup> atc agc gtt tat		633
Tyr Ile Arg Glu Arg Phe Asp Asn Glu Thr Phe Arg Ile Ser Val Tyr		
180	185	190
cag gtg ctc cag gag cac ttg gg <sup>c</sup> agg gaa tcg gat ctc ttc ctg ctc		681
Gln Val Leu Gln Glu His Leu Gly Arg Glu Ser Asp Leu Phe Leu Leu		
200	205	210
gac agc cgt acc ctc tgg gcc tcg gag gag gg <sup>c</sup> tgg ctg gtg ttt gac		729
Asp Ser Arg Thr Leu Trp Ala Ser Glu Glu Gly Trp Leu Val Phe Asp		
215	220	225
atc aca gcc acc agc aac cac tgg gtg gtc aat ccg cg <sup>c</sup> cac aac ctg		777
Ile Thr Ala Thr Ser Asn His Trp Val Val Asn Pro Arg His Asn Leu		
230	235	240

ggc ctg cag ctc tcg gtg gag acg ctg gat ggg cag agc atc aac ccc			825
Gly Leu Gln Leu Ser Val Glu Thr Leu Asp Gly Gln Ser Ile Asn Pro			
245	250	255	
aag ttg gcg ggc ctg att ggg cg <sup>g</sup> cac ggg ccc cag aac aag cag ccc			873
Lys Leu Ala Gly Leu Ile Gly Arg His Gly Pro Gln Asn Lys Gln Pro			
260	265	270	275
ttc atg gtg gct ttc ttc aag gcc acg gag gtc cac ttc cgc agc atc			921
Phe Met Val Ala Phe Phe Lys Ala Thr Glu Val His Phe Arg Ser Ile			
280	285	290	
cgg tcc acg ggg agc aaa cag cgc agc cag aac cgc tcc aag acg ccc			969
Arg Ser Thr Gly Ser Lys Gln Arg Ser Gln Asn Arg Ser Lys Thr Pro			
295	300	305	
aag aac cag gaa gcc ctg cgg atg gcc aac gtg gca gag aac agc agc			1017
Lys Asn Gln Glu Ala Leu Arg Met Ala Asn Val Ala Glu Asn Ser Ser			
310	315	320	
agc gac cag agg cag gcc tgt aag aag cac gag ctg tat gtc agc ttc			1065
Ser Asp Gln Arg Gln Ala Cys Lys Lys His Glu Leu Tyr Val Ser Phe			
325	330	335	
cga gac ctg ggc tgg cag gac tgg atc atc gc <sup>g</sup> cct gaa ggc tac gcc			1113
Arg Asp Leu Gly Trp Gln Asp Trp Ile Ile Ala Pro Glu Gly Tyr Ala			
340	345	350	355
gcc tac tac tgt gag ggg gag tgt gcc ttc cct ctg aac tcc tac atg			1161
Ala Tyr Tyr Cys Glu Gly Glu Cys Ala Phe Pro Leu Asn Ser Tyr Met			
360	365	370	
aac gcc acc aac cac gcc atc gtg cag acg ctg gtc cac ttc atc aac			1209
Asn Ala Thr Asn His Ala Ile Val Gln Thr Leu Val His Phe Ile Asn			
375	380	385	
ccg gaa acg gtg ccc aag ccc tgc tgt gc <sup>g</sup> ccc acg cag ctc aat gcc			1257
Pro Glu Thr Val Pro Lys Pro Cys Cys Ala Pro Thr Gln Leu Asn Ala			
390	395	400	
atc tcc gtc ctc tac ttc gat gac agc tcc aac gtc atc ctg aag aaa			1305
Ile Ser Val Leu Tyr Phe Asp Asp Ser Ser Asn Val Ile Leu Lys Lys			
405	410	415	
tac aga aac atg gtg gtc cgg gcc tgt ggc tgc cac tagctcctcc			1351
Tyr Arg Asn Met Val Val Arg Ala Cys Gly Cys His			
420	425	430	

gagaattcag accctttggg gccaagttt tctggatcct ccattgctcg ccttggccag 1411  
gaaccagcag accaactgcc ttttgtgaga ccttcccctc cctatccccca actttaaagg 1471  
tgtgagagta ttaggaaaca tgagcagcat atggctttg atcagtttt cagtggcagc ,1531  
atccaatgaa caagatccta caagctgtgc aggcaaaacc tagcagaaaa aaaaaacaac 1591  
gcataaagaa aaatggccgg gccaggtcat tggctggaa gtctcagcca tgcacggact 1651  
cgtttccaga ggtaattatg agcgcctacc agccaggcca cccagccgtg ggaggaagg 1711  
ggcgtggcaa ggggtggca cattggtgtc tgtgcgaaag gaaaattgac ccgaaagttc 1771  
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<211> 431  
<212> PRT  
<213> Homo sapiens

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Leu Trp Ala Pro Leu Phe Leu Leu Arg Ser Ala Leu Ala Asp Phe Ser  
20 25 30  
  
Leu Asp Asn Glu Val His Ser Ser Phe Ile His Arg Arg Leu Arg Ser  
35 40 45  
  
Gln Glu Arg Arg Glu Met Gln Arg Glu Ile Leu Ser Ile Leu Gly Leu  
50 55 60  
  
Pro His Arg Pro Arg Pro His Leu Gln Gly Lys His Asn Ser Ala Pro  
65 70 75 80  
  
Met Phe Met Leu Asp Leu Tyr Asn Ala Met Ala Val Glu Glu Gly Gly  
85 90 95  
  
Gly Pro Gly Gly Gln Gly Phe Ser Tyr Pro Tyr Lys Ala Val Phe Ser  
100 105 110  
  
Thr Gln Gly Pro Pro Leu Ala Ser Leu Gln Asp Ser His Phe Leu Thr  
115 120 125

Asp Ala Asp Met Val Met Ser Phe Val Asn Leu Val Glu His Asp Lys  
130 135 140

Glu Phe Phe His Pro Arg Tyr His His Arg Glu Phe Arg Phe Asp Leu  
145 150 155 160

Ser Lys Ile Pro Glu Gly Glu Ala Val Thr Ala Ala Glu Phe Arg Ile  
165 170 175

Tyr Lys Asp Tyr Ile Arg Glu Arg Phe Asp Asn Glu Thr Phe Arg Ile  
180 185 190

Ser Val Tyr Gln Val Leu Gln Glu His Leu Gly Arg Glu Ser Asp Leu  
195 200 205

Phe Leu Leu Asp Ser Arg Thr Leu Trp Ala Ser Glu Glu Gly Trp Leu  
210 215 220

Val Phe Asp Ile Thr Ala Thr Ser Asn His Trp Val Val Asn Pro Arg  
225 230 235 240

His Asn Leu Gly Leu Gln Leu Ser Val Glu Thr Leu Asp Gly Gln Ser  
245 250 255

Ile Asn Pro Lys Leu Ala Gly Leu Ile Gly Arg His Gly Pro Gln Asn  
260 265 270

Lys Gln Pro Phe Met Val Ala Phe Phe Lys Ala Thr Glu Val His Phe  
275 280 285

Arg Ser Ile Arg Ser Thr Gly Ser Lys Gln Arg Ser Gln Asn Arg Ser  
290 295 300

Lys Thr Pro Lys Asn Gln Glu Ala Leu Arg Met Ala Asn Val Ala Glu  
305 310 315 320

Asn Ser Ser Ser Asp Gln Arg Gln Ala Cys Lys Lys His Glu Leu Tyr  
325 330 335

Val Ser Phe Arg Asp Leu Gly Trp Gln Asp Trp Ile Ile Ala Pro Glu  
340 345 350

Gly Tyr Ala Ala Tyr Tyr Cys Glu Gly Glu Cys Ala Phe Pro Leu Asn  
355 360 365

Ser Tyr Met Asn Ala Thr Asn His Ala Ile Val Gln Thr Leu Val His  
370 375 380

Phe Ile Asn Pro Glu Thr Val Pro Lys Pro Cys Cys Ala Pro Thr Gln  
385                    390                    395                    400

Leu Asn Ala Ile Ser Val Leu Tyr Phe Asp Asp Ser Ser Asn Val Ile  
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<212> PRT

<213> Artificial Sequence

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<223> Description of Artificial Sequence: OPX -  
Consensus sequence

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<223> Wherein Xaa is independently selected from a group  
of one or more specified amino acids as defined in  
the specification

<400> 3

Cys Xaa Xaa His Glu Leu Tyr Val Xaa Phe Xaa Asp Leu Gly Trp Xaa  
1                    5                    10                    15

Asp Trp Xaa Ile Ala Pro Xaa Gly Tyr Xaa Ala Tyr Tyr Cys Glu Gly  
20                    25                    30

Glu Cys Xaa Phe Pro Leu Xaa Ser Xaa Met Asn Ala Thr Asn His Ala  
35                    40                    45

Ile Xaa Gln Xaa Leu Val His Xaa Xaa Xaa Pro Xaa Xaa Val Pro Lys  
50                    55                    60

Xaa Cys Cys Ala Pro Thr Xaa Leu Xaa Ala Xaa Ser Val Leu Tyr Xaa  
65                    70                    75                    80

Asp Xaa Ser Xaa Asn Val Xaa Leu Xaa Lys Xaa Arg Asn Met Val Val  
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Xaa Ala Cys Gly Cys His  
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<223> Description of Artificial Sequence: Generic
      Sequence 7

<220>
<223> Wherein Xaa is independently selected from a group
      of one or more specified amino acids as defined in
      the specification

<400> 4
Leu Xaa Xaa Xaa Phe Xaa Xaa Xaa Gly Trp Xaa Xaa Xaa Xaa Xaa Xaa
  1           5           10          15

Pro Xaa Xaa Xaa Xaa Ala Xaa Tyr Cys Xaa Gly Xaa Cys Xaa Xaa Pro
  20          25          30

Xaa Xaa Xaa Xaa Xaa Xaa Xaa Asn His Ala Xaa Xaa Xaa Xaa Xaa
  35          40          45

Xaa Cys Cys Xaa Pro
  50          55          60

Xaa Xaa Xaa Xaa Xaa Xaa Xaa Leu Xaa Xaa Xaa Xaa Xaa Xaa Xaa Xaa
  65          70          75          80

Val Xaa Leu Xaa Xaa Xaa Xaa Met Xaa Val Xaa Xaa Cys Xaa Cys
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Xaa

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<210> 5
<211> 102
<212> PRT
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<223> Description of Artificial Sequence: Generic
      Sequence 8

<220>
<223> Wherein Xaa is independently selected from a group

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of one or more specified amino acids as defined in  
the specification

<400> 5

Cys Xaa Xaa Xaa Xaa Leu Xaa Xaa Xaa Phe Xaa Xaa Xaa Gly Trp Xaa  
1 5 10 15

Xaa Xaa Xaa Xaa Xaa Pro Xaa Xaa Xaa Xaa Ala Xaa Tyr Cys Xaa Gly  
20 25 30

Xaa Cys Xaa Xaa Pro Xaa Xaa Xaa Xaa Xaa Xaa Xaa Asn His Ala  
35 40 45

Xaa  
50 55 60

Xaa Cys Cys Xaa Pro Xaa Xaa Xaa Xaa Xaa Xaa Xaa Xaa Leu Xaa Xaa  
65 70 75 80

Xaa Xaa Xaa Xaa Xaa Val Xaa Leu Xaa Xaa Xaa Xaa Met Xaa Val  
85 90 95

Xaa Xaa Cys Xaa Cys Xaa  
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<210> 6

<211> 97

<212> PRT

<213> Artificial Sequence

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Xaa  
1 5 10 15

Pro Xaa Xaa Xaa Xaa Xaa Xaa Cys Xaa Gly Xaa Cys Xaa Xaa Xaa  
20 25 30

Xaa Xaa

35

40

45

Xaa Cys Xaa Pro  
50 55 60

Xaa Xaa Xaa Xaa Xaa Xaa Xaa Leu Xaa Xaa Xaa Xaa Xaa Xaa Xaa  
65 70 75 80

Xaa Cys Xaa Cys  
85 90 95

Xaa

<210> 7  
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<212> PRT  
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<220>  
<223> Description of Artificial Sequence: Generic  
Sequence 10

<220>  
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<400> 7  
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1 5 10 15

Xaa Xaa Xaa Xaa Xaa Pro Xaa Xaa Xaa Xaa Xaa Xaa Xaa Cys Xaa Gly  
20 25 30

Xaa Cys Xaa  
35 40 45

Xaa  
50 55 60

Xaa Xaa Cys Xaa Pro Xaa Xaa Xaa Xaa Xaa Xaa Xaa Xaa Leu Xaa Xaa  
65 70 75 80

Xaa  
85 90 95

Xaa Xaa Cys Xaa Cys Xaa

100

<210> 8

<211> 5

<212> PRT

<213> Artificial Sequence

<220>

<223> Description of Artificial Sequence: Fragment

Sequence that can be placed at the N-terminus of

Generic Sequence 8

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<223> Wherein Xaa is independently selected from a group  
of one or more specified amino acids as defined in  
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<400> 8

Cys Xaa Xaa Xaa Xaa

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<210> 9

<211> 5

<212> PRT

<213> Artificial Sequence

<220>

<223> Description of Artificial Sequence: Fragment

Sequence that can be placed at the N-terminus of

Generic Sequence 9

<220>

<223> Wherein Xaa is independently selected from a group  
of one or more specified amino acids as defined in  
the specification

<400> 9

Cys Xaa Xaa Xaa Xaa

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